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Millions of people are living with lasting effects of COVID-19.

# TALLYING THE HEALTH TOLL OF COVID-19

Researchers are trying to calculate the burden of infection and its after-effects. **By Holly Else**

**H**ow do you count the cost of a pandemic? COVID-19 has killed an estimated 15 million people since it emerged at the end of 2019, but its impact on health reaches much further. For hundreds of millions of people around the world, infection with the coronavirus SARS-CoV-2

has brought a range of problems, from the acute effects of the illness to the lasting symptoms known as long COVID.

Working out the size of that health burden is challenging, but important – governments use such figures to plan how to spend health-care budgets. So researchers are starting to tally the overall health impacts and trying to draw

lessons from any patterns. They're hoping, for example, to discern how different populations are affected and to provide evidence about the effects of vaccine roll-outs and new variants of the virus.

Even without a pandemic, there is no easy way to tally all the effects of various health conditions: good data can be hard to come by

and decisions on how to measure burdens are inherently subjective. “There are a whole lot of social value choices where there isn’t hard science,” says Theo Vos, an epidemiologist at the Institute for Health Metrics and Evaluation (IHME) at the University of Washington in Seattle, a research centre that aims to categorize the global health burden of diseases. “How do you value a year with asthma, a year without a leg, a year with depression?”

Those calculations are even harder when scientists are grappling with a new virus and a poorly characterized disease.

Research groups are exploring a number of ways to calculate the burden of COVID-19, and many are starting to report their results. Early data suggest that the impact is significant and varies by country. One study found that COVID-19 took a heavy toll across 16 European countries, but that the impacts on different nations varied owing to factors ranging from the population’s age structure to political responses to the pandemic<sup>1</sup> (see ‘A heavy burden’).

Estimates produced by national teams provide more detail. In Scotland<sup>2</sup>, COVID-19 was second only to ischaemic heart disease in terms of the impact it had on the population’s health in 2020. In the Netherlands<sup>3</sup> that year, the burden was 16 times that of a typical influenza season, according to a preprint published last November.

With the pandemic still raging across many parts of the world, it’s too early to calculate the full toll. But some researchers think it has helped to change how they calculate the health effects of diseases. “The pandemic has strengthened collaborations in the field of disease burden,” says Sara Monteiro Pires, an epidemiologist at the Technical University of Denmark. Researchers are now harmonizing the processes they use to estimate disease burden, and tailoring the models to the data available in each location. They hope this will make the results more precise.

### Adding up the effects

The UK National Health Service lists a dozen COVID-19 symptoms for adults, from loss of smell to a high temperature. Even people who have a relatively mild case and ride out the symptoms at home can see lasting health effects, such as fatigue or shortness of breath. If symptoms continue beyond a couple of months, people can be diagnosed with an illness widely known as long COVID.

To quantify how a disease affects an entire population, scientists combine data on individual experiences. These include the number of people infected, the number who had certain symptoms, the length of illnesses, how many needed hospital treatment or died, and patients’ ages, among other things. They then use them to work out how many years of life have been lost to the disease and how many

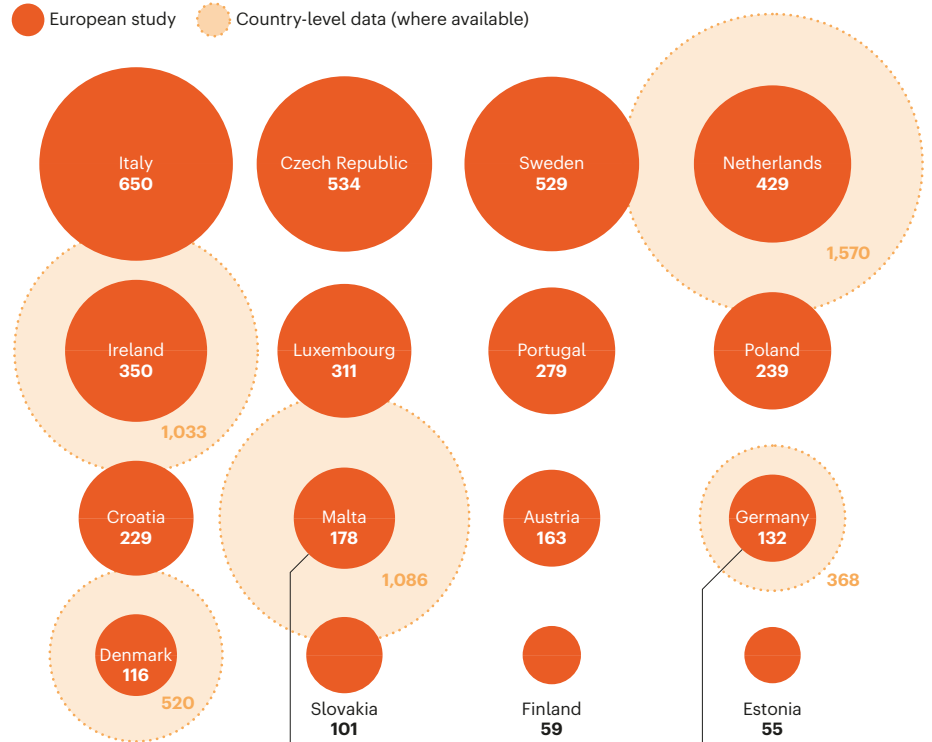
# A HEAVY BURDEN

Researchers are starting to analyse how many years of life have been lost to death and ill health from COVID-19, measured in units called disability-adjusted life years (DALYs).

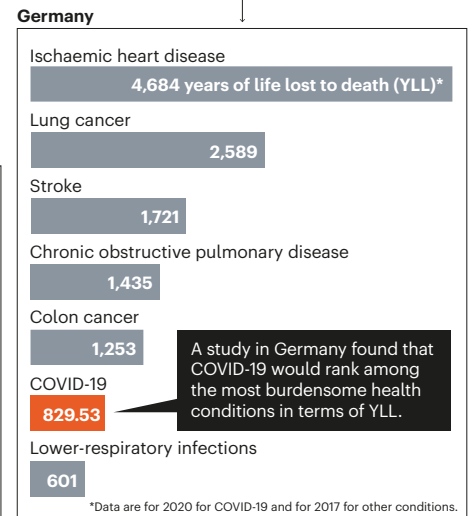
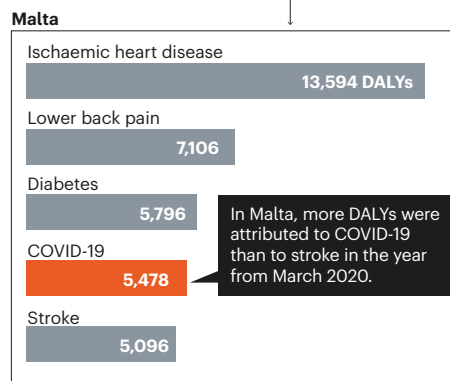
### The toll of COVID-19 in Europe

An analysis of 16 European countries using data from sources such as the World Health Organization suggests that the toll can vary widely depending on a population’s age structure or, perhaps, a government’s response to the pandemic. National estimates, using more detailed data, tend to yield larger burden estimates.

COVID-19 DALYs per 100,000 people (data for 2020):



**How COVID-19 stacks up**  
In countries for which data are available, COVID-19 tends to be one of the most burdensome diseases.



years are lived with disabling symptoms.

Researchers can use the average life expectancies in a country to work out how many years of life have been lost owing to premature death. Losses due to disability are harder to calculate, however. To quantify those, researchers use data about the number of people affected by a certain illness, the length of time they have it and a value for the illness known as a disability weight. The IHME’s Global Burden of Disease group maintains a

standardized list of disability weights; the latest version available, published in 2019, gives a mild earache a disability weight of 0.013 and severe multiple sclerosis 0.719 (a weight of 0 is perfect health; a weight of 1 is death).

Currently, there is no standardized disability weight for COVID-19. Instead, researchers use the disability weights associated with other infectious diseases and similar health conditions.

Totalling the years of life lost due to



illness, disability or premature death gives an estimate of the burden in a unit known as disability-adjusted life years, or DALYs. It is the keystone of research into the burden of disease.

The data that go into DALYs come from a variety of sources. Many are routinely collected by national health authorities. For COVID-19, some data have been gathered through targeted surveillance efforts such as the REACT study (Real-time Assessment of Community Transmission), a massive sampling exercise that began in 2020 and has chronicled how SARS-CoV-2 is moving through England and what symptoms people are experiencing.

Data from the REACT study suggest that COVID-19's health effects can linger. A preprint posted on the medRxiv server last July suggested that 19% of the English population had had COVID-19, and that around one-third of those – more than 2 million adults – had experienced one or more symptoms for at least 12 weeks<sup>4</sup>. “That’s 6% of the population,” says Paul Elliot, an epidemiologist at Imperial College London, who leads the REACT study and co-authored the study.

Max Taquet, a clinical researcher and engineer at the University of Oxford, UK, who uses data from medical records to understand the neurological and psychiatric consequences of COVID-19, says that estimating the health effects of long COVID is difficult and that the numbers are startling. “Many of us were surprised of the scale of the problem,” he says, “but we do see this [post-infection syndrome] with other viral infections”. With COVID-19, scientists are monitoring the consequences in real time. “It’s great that we are finally paying attention to it.”

There is no guarantee that these data sources will stick around, however. The UK government announced in March that it would be stopping funding for some branches of the REACT study and for another surveillance effort.

### Big burden

Early results on the health lost to COVID-19 are trickling in. “Overall, the impact of COVID-19 has been dramatically high worldwide,” says Gianfranco Politano, a bioinformatician at the Polytechnic University of Turin in Italy, who was involved in the study of 16 European countries.

The European research suggests that Slovakia probably had a lower burden than other countries because the government acted quickly to lock down and people complied. By contrast, the burden was higher in Sweden, where the government took a “herd immunity” approach and allowed the virus to spread largely unchecked.

Individual-country analyses also reveal big differences in the health burden of COVID-19. Research from Malta reveals that between

March 2020 and March 2021, COVID-19 became the fourth leading cause of disability, ranking after ischaemic heart disease, lower back pain and diabetes<sup>5</sup>. In India, it ranked much further down the list: using 2019 data as a guide, it would have accounted for 3% of the total health burden – putting it outside the top 10 and rating it as less of a burden than ischaemic heart disease, nutritional deficiencies and chronic respiratory diseases<sup>6</sup>. The authors acknowledge, however, that COVID-19 cases might be under-reported in India, which would affect the rate of DALYs.



**IT'S A SIZEABLE PROBLEM, THESE ARE PEOPLE WHO ARE PRETTY SEVERELY DISABLED.”**

Each project sources its data slightly differently, which can add to the variation in DALY estimations. The research group that estimated DALYs for 16 European countries, for example, used aggregated data from the European Centre for Disease Prevention and Control (ECDC), the World Health Organization (WHO) and the World Bank Group; many of the national studies used more-detailed country-specific data. As a consequence, DALY estimates for the same country vary in different hands. Using ECDC, WHO and World Bank data for Denmark, for example, gives a figure of 116 DALYs per 100,000 people<sup>1</sup>, whereas Monteiro Pires' group used data from Denmark's health systems to come up with a figure closer to 520 (see [go.nature.com/3m6nsrj](https://go.nature.com/3m6nsrj)).

Several of the studies of individual European countries have been supported by the European Burden of Disease Network, a project launched in 2019 to improve how the burden of disease is calculated and understood. The network of epidemiologists and public-health researchers from 53 countries worldwide quickly realized that it should be documenting the public-health burden of the nascent pandemic virus, and began to develop a consensus protocol, including a specific model for the disease progression of COVID-19 from infection to recovery or death. “From that moment on, many countries have been using that protocol. We never imagined it would happen so quickly,” says Monteiro Pires, who heads the network's infectious-disease working group. Network researchers have now completed burden estimates for Malta, Denmark, the Netherlands, Scotland, Ireland and Germany, with

more expected to appear in the months ahead.

One important job for the network was to align the definitions used in the data sets so that the burdens of disease could be compared across countries. But it is still too soon to draw any major conclusions from the work, says Monteiro Pires.

There is not yet an estimate of the global health toll from COVID-19, but the IHME has been churning out figures for a catalogue of other diseases since the 1990s. In early 2020, when it became clear a pandemic was under way, the institute already had the machinery in place to help it understand the wider health effects of SARS-CoV-2 and got to work on adding COVID-19 to the catalogue. Around 100 staff members were diverted to the effort. Their data are currently being considered for publication.

In contrast to many other calculations, the data include estimates of the burden of long COVID. Vos has presented these unpublished data to US authorities to help them get a handle on how the lingering symptoms could affect people's ability to work. The findings suggest that in 2020 and 2021, an estimated 4.6 million people in the United States had symptoms that persisted for at least three months. The group's definition of long COVID revolves around three clusters of symptoms, centring on fatigue, cognitive problems and ongoing respiratory issues. More than 85% of these cases came as a result of a bout of COVID-19 that did not require hospital treatment.

“It's a sizeable problem, these are people who are pretty severely disabled,” says Vos.

The team's modelling suggests that around 5% of women and 2% of men who had a mild case of COVID-19 still had symptoms 6 months after the acute phase of the illness ended. For those treated in hospital, it was 26% of women and 15% of men, rising to 42% and 27%, respectively, if the patient spent time in the intensive care unit.

Vos' team found that people with long COVID had an average disability weight of 0.21 – equivalent to complete hearing loss or severe traumatic brain injury. “Hopefully this will trigger awareness with treating physicians that this is not trivial and it does exist,” Vos adds.

### Data gaps

One big problem for researchers attempting to estimate the burden of COVID-19 is the coverage of data. Some countries, such as those in the Pacific Islands, record so few cases that the data are not statistically sound. And many countries in sub-Saharan Africa, among other regions, lack the ability to track excess deaths due to COVID because of inadequate registration systems.

The IHME group get around this by using data from neighbouring countries to generate country-specific estimates. But ultimately,



A woman who has had COVID-19 attends a physiotherapy session in Madrid.

accurate calculations will require the collection of more detailed data. “People don’t automatically think that improving information systems is a priority in a pandemic,” says Andrew Briggs, a health economist at the London School of Hygiene & Tropical Medicine, “but in terms of preparedness we should be.” He and his colleague Anna Vassall recently predicted that as much as 30% of the health burden of COVID-19 could be down to disability<sup>7</sup>, not death.

The second data blind spot is long COVID. So far, only a few research groups outside the IHME have included such data in their estimates. Others think that without good information on long COVID, calculating the burden of the disease is premature.

Some national estimates – such as those for Scotland<sup>2</sup>, Malta<sup>5</sup> and Ireland<sup>6</sup> – include limited long-COVID data in their analyses, but acknowledge the uncertainties. Grant Wyper, who works on the burden of disease for Public Health Scotland, helped to put together these estimates and says that the data on long COVID were sparse and that the condition was often defined in different ways – combining data from people who had just one symptom, such as loss of sense of smell, with those from people who had several symptoms, which would have a more severe impact on quality of life.

Because so little was known when they developed the initial disease model, Wyper and his group used a general disability weight

for the health effects seen after an infection. They are now working to refine the disability weighting for long COVID to make it more accurate, he says.

For its estimates of the burden of long COVID, the IHME sought out ongoing cohort studies that were logging symptoms and, in some instances, assessments of general health before COVID-19 developed. Its model pulls together data from 10 cohorts worldwide and includes more than 5,000 people treated in the community or hospital, as well as data from medical records and published studies.

But the estimates rely on the assumption that people who do not have symptoms during the acute phase do not develop long COVID. Taquet says that it is not yet clear that this is the case. “There is no reason to believe that someone with no symptoms at the time of the acute infection won’t go on to develop symptoms of long COVID later on,” he adds. His team has found that 2 in every 5 people with long COVID symptoms 3–6 months after infection did not report symptoms in the first 3 months<sup>9</sup>.

Some groups might be disproportionately affected by COVID-19. Briggs and Vassall stress that the data should be collected in a way that is sensitive to that, and broken down by age, socioeconomic and ethnic group. “As we move to an endemic situation, we have got to be more concerned by equity,” he says. For its part, the European Burden of Disease Network is hoping to look at how social inequality

affects health burden in the future.

Measuring DALYs takes time – often the analyses are done only once a year. That means that some key questions about the burden of COVID-19 – such as how vaccines have affected illness rates and severity – won’t be answered for a while. The fact that COVID-19 has been around for only a couple of years means that scientists don’t have enough data to make accurate forecasts, says Maria Gianino, an economist at the University of Turin, who worked on the study of 16 European countries.

Despite the challenges, Monteiro Pires thinks that the future for disease-burden studies is bright. More funding is coming their way, she says. “It is more acknowledged that this is an important tool for public health”.

**Holly Else** reports for *Nature* from London.

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